

AMENDMENTS TO THE SPECIFICATION

Please amend paragraph 93 on page 20 as follows:

--Figure 22 Figures 22A and 22B are is a graphical representation representations showing a time-course similar to that described in Figure 15. BTY1N4 represents the EYFP reporter, with both protein- and mRNA-destabilising elements as described in Figure 18. BTpuroY1N4 was constructed by inserting the puromycin coding sequence, in frame, at the 5' end of the coding sequence in BTY1N4, such that the reporter protein produced is a fusion of the puromycin-resistance protein, EYFP and the MODC destabilising sequence. As seen in Figure 18, reporter levels from BTY1N4 decay rapidly after doxycycline (drug). As shown in Figure 22A, A a similar rate of decay was seen with the puromycin-fusion reporter, either when expressed transiently (BTpuroY1N4) or stably (BTpuroY1N4 stable cell line). The fact that we were able to select a stable cell line in puromycin shows that the puromycin resistance gene is active in this fusion protein and the detectable levels of fluorescence show that the EYFP component maintains fluorescent activity. The decay curves demonstrate that rapid decay of our destabilised reporters is reproducible in stably transfected cells and is not compromised with the fusion protein. Similarly, the neomycin-EYFP-MODC fusion protein (BTneoY1N4) also conferred antibiotic resistance (not shown) and expressed detectable levels of fluorescence that decayed rapidly after drug. Figure 22B shows a similar but separate experiment utilising the same BTY1N4 and BTpuroY1N4 constructs. The wild-type ubiquitin sequence, followed by an arginine was cloned in frame and upstream of the coding sequence in these vectors to create BTuY1N4 and BTupuroY1N4 respectively. Upon translation of these reporters, the ubiquitin polypeptide is cleaved, to create a reporter protein with an N-terminal arginine and associated leader sequence that directs decay via the N-end rule. In particular, BTuY1N4 decayed extremely fast, reaching 50% of initial values after only ~1.7 hrs. This demonstrates that enhanced decay can be achieved by incorporating 2 different protein degradation signals.--.